



**QUEEN'S
UNIVERSITY
BELFAST**

Time-dependent behaviour of bone accentuates loosening in the fixation of fractures using bone-screw systems

Xie, S., Manda, K., & Pankaj, P. (2018). Time-dependent behaviour of bone accentuates loosening in the fixation of fractures using bone-screw systems. *Bone and Joint Research*, 7(10), 580-586. <https://doi.org/10.1302/2046-3758.710.BJR-2018-0085.R1>

Published in:
Bone and Joint Research

Document Version:
Publisher's PDF, also known as Version of record

Queen's University Belfast - Research Portal:
[Link to publication record in Queen's University Belfast Research Portal](#)

Publisher rights
Copyright 2018 the authors.
This is an open access article published under a Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution and reproduction in any medium, provided the author and source are cited.

General rights
Copyright for the publications made accessible via the Queen's University Belfast Research Portal is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The Research Portal is Queen's institutional repository that provides access to Queen's research output. Every effort has been made to ensure that content in the Research Portal does not infringe any person's rights, or applicable UK laws. If you discover content in the Research Portal that you believe breaches copyright or violates any law, please contact openaccess@qub.ac.uk.

BJR



■ BIOMECHANICS

Time-dependent behaviour of bone accentuates loosening in the fixation of fractures using bone-screw systems

**S. Xie,
K. Manda,
P. Pankaj**

*The University of
Edinburgh, Edinburgh,
United Kingdom*

Aims

Loosening is a well-known complication in the fixation of fractures using devices such as locking plates or unilateral fixators. It is believed that high strains in the bone at the bone-screw interface can initiate loosening, which can result in infection, and further loosening. Here, we present a new theory of loosening of implants. The time-dependent response of bone subjected to loads results in interfacial deformations in the bone which accumulate with cyclical loading and thus accentuates loosening.

Methods

We used an 'ideal' bone-screw system, in which the screw is subjected to cyclical lateral loads and trabecular bone is modelled as non-linear viscoelastic and non-linear viscoelastic-viscoplastic material, based on recent experiments, which we conducted.

Results

We found that the interfacial deformation in the bone increases with the number of cycles, and the use of a non-linear viscoelastic-viscoplastic model results in larger deformations, some of which are irrecoverable. There is an apparent trend in which interfacial deformations increase with increasing porosity of bone.

Conclusion

The developed time-dependent model of the mechanical behaviour of bone permits prediction of loosening due to cyclical loads, which has not been possible previously. Application of this model shows that implant loosening will be accentuated by cyclical loading due to physiological activities, and the risks of loosening are greater in osteoporotic patients.

Cite this article: *Bone Joint Res* 2018;7:580–586.

Keywords: Cyclical loading, Viscoelastic-viscoplastic, Bone volume ratio, Irrecoverable strain

Article focus

- The effect of the time-dependent behaviour of bone at the bone-screw interface is examined.
- Viscoelastic and viscoplastic models are used to simulate behaviour of an idealized bone-screw system subjected to cyclical loading.

Key messages

- The simulations show that deformations at the bone-screw interface accumulate with cyclical loading.
- Interfacial deformations increase with increasing bone porosity.

Strengths and limitations

- We incorporate, for the first time, non-linear viscoelastic and non-linear

viscoelastic-viscoplastic material properties in finite element simulations for trabecular bone.

- Microstructural anisotropy is likely to play an important role but is not included in this study.

Introduction

Many forms of fracture-fixation treatments, such as unilateral fixators and locking plates, employ uni- or bi-cortical screws, which traverse the bone and permit load transfer across fractured segments.¹ The bone-fixator construct can fail due to breakage of the device, such as a screw or a plate, which can occur due to fatigue, particularly when healing is delayed. Another common mode of failure follows loosening of a screw or screws. This

■ S. Xie, PhD, Postdoctoral Researcher, School of Engineering, Institute for Bioengineering, The University of Edinburgh, Edinburgh, UK.

■ K. Manda, PhD, Lecturer, School of Mechanical and Aerospace Engineering, Queen's University Belfast, Belfast, UK.

■ P. Pankaj, PhD, Professor of Computational Biomechanics, School of Engineering, Institute for Bioengineering, The University of Edinburgh, Edinburgh, UK.

Correspondence should be sent to P. Pankaj; email: pankaj@ed.ac.uk

doi: 10.1302/2046-3758.710.
BJR-2018-0085.R1

Bone Joint Res 2018;7:580–586.

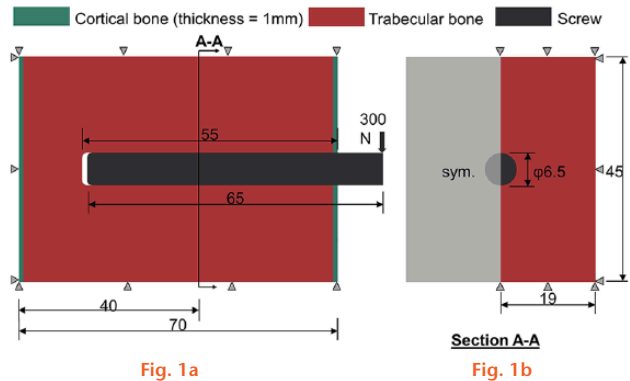


Fig. 1a

Fig. 1b

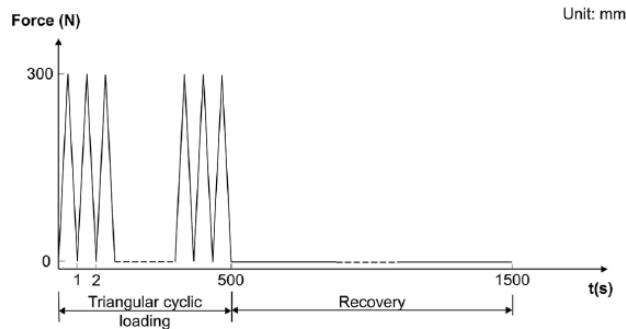


Fig. 1c

The geometry of the bone-screw system showing a symmetry surface with location of the application of load (a); section A-A (b); load application - each model was subjected to 500 cycles of triangular load of 300 N amplitude followed by 1000 s of recovery (c).

has been reported frequently, and it has previously been noted that this is usually initiated by mechanical forces before any contribution from biological processes.² It has been suggested that screw loosening and failure, observed clinically, probably results from bone-screw separation events and from elevated strains.³ The bone yields locally at the interface due to high stresses or strains, and this initiates loosening, which may lead to infection, and further loosening.⁴⁻⁶

Most orthopaedic implants have some form of load-sharing arrangement with the bone which cause cyclical stresses and strains at the bone-implant interface due to physiological activities. Experimental investigations have shown that the separation is a function of the number of cycles for a range of implants, including pedicle screws,^{7,8} dynamic hip screws,⁹ and the fixation of distal tibial^{10,11} and distal radial fractures.¹² A study on dental implants drew attention to the fact that repeated loading-unloading cycles result in alternating compression and separation of the bone-screw interface.³ The nature of migration suggests that it is a mechanical phenomenon, or at least mechanically triggered, rather than a purely biological process.²

In computational modelling, loosening at the interface has, in the past, been examined by evaluating the level of strain after using time-independent elastic⁷ or

elastoplastic^{4,8} constitutive models for bone. On the other hand, it is recognized that the response of bone to loads is time-dependent⁹ and some permanent deformation arises even at low levels of strain ($<3000 \mu\epsilon$).^{10,11} It has also been shown that, similar to time-independent material properties such as Young's modulus, time-dependent properties are also related to the bone volume fraction (BV/TV).^{12,13} However, these time-dependent mechanical properties of bone are not generally incorporated in modelling.¹⁴

The aim of this study was to examine possible loosening due to cyclical loading in an idealized bone-screw system in which trabecular bone is assigned time-dependent non-linear viscoelastic and non-linear viscoelastic-viscoplastic properties. The properties which were used are based on recent experiments and constitutive models.¹⁵ Our hypothesis was that bone-screw systems used in the fixation of fractures can become loose when subjected to cyclical loading due to time-dependent mechanical properties of bone, and the rate of loosening is associated with the BV/TV.

Materials and Methods

In designing the study, we considered a screw inserted in a block of bone subjected to lateral cyclical loads, as shown in Figure 1a, which also shows the dimensions. The dimensions of the screw are similar to those used in locking plates. Taking advantage of symmetry, only half of the bone block-screw system was modelled (Fig. 1b). Exact fit between the screw and the bone was considered at the interface between the circumference of the screw and the bone, while a small gap was assumed between the tip of the screw and bone to avoid influence of any end-shape effects, and to maintain simplicity. A frictional screw-bone interface was used with a standard Coulomb friction coefficient of 0.3.^{16,17} The threads of the screw were excluded. The screw was assumed to be unicortical and a 1 mm thick cortex was included in the model (Fig. 1a).

All external faces of the block were assumed to be fully restrained except for the face with the screw hole, and symmetry boundary conditions were applied at the symmetry surface (Figs 1a and 1b). Triangular cyclic forces with an amplitude of 300 N and a frequency, 1 Hz, as shown in Figure 1c, were applied to the external end of the screw (Fig. 1a). The models were permitted 1000 seconds of recovery after 500 complete cycles, as shown in Figure 1c. We chose 500 cycles as we were mainly interested in evaluating the trends, though this choice was also partly dictated by the computational resources required for this highly non-linear problem.

The screw and the cortical bone were modelled as linear elastic time-independent materials, with Young's moduli of 180 GPa and 20.7 GPa, respectively,¹⁶ and a Poisson's ratio of 0.3. Trabecular bone was modelled

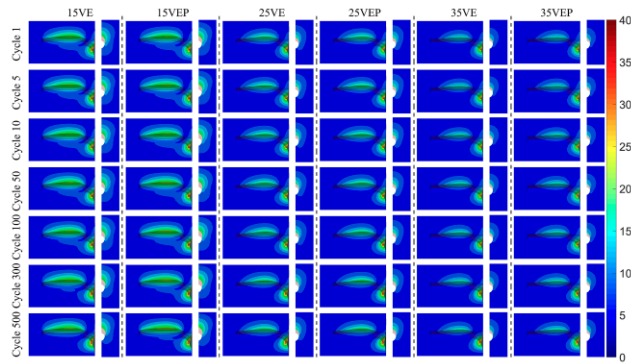


Fig. 2a

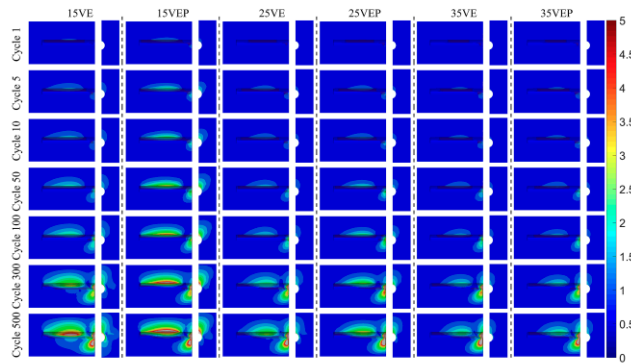


Fig. 2b

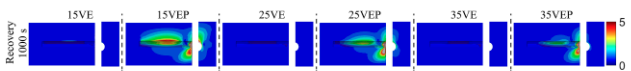


Fig. 2c

The displacement (μm) contours at the symmetry surface and section A-A for seven representative cycles when load at its peak (300 N) (a); when load is zero (b) and recovery after 1000 seconds (c). They are magnified $\times 150$, and the section plots are superimposed with undeformed geometry for better comparison with its original shape.

using two models: a non-linear viscoelastic (VE) model and a non-linear viscoelastic-viscoplastic (VEP) model. The mathematical details of these models are provided as supplementary information, which include data for each of the three BV/TV values considered.

The screw-bone system was modelled in Abaqus (v6.12; Dassault Systèmes Simulia, Providence, Rhode Island), using 13,182 3D finite elements (brick, C3D8 and tetrahedron, C3D10M). Mesh convergence studies were performed and they showed that further refinement resulted in a change of peak displacement of bone by $< 0.5\%$.

Results

Trabecular bone displacements and strains in the region around the screw were compared at three stages for different cycles: timepoints when the load is at its peak (300 N); timepoints when the load is zero; and at the end of the recovery (at the end of 1000 seconds after loading is stopped). In Figure 2, the rows present displacement

contours at different stages and cycles. The columns are for different samples of bone, with numerals indicating BV/TV percentage of the samples, and for the two time-dependent material models used (VE and VEP). For each case, contours along the length of the screw (Fig. 1a) and at the symmetry surface, section A-A (Fig. 1b), are shown in Figure 2. The displacements were magnified $\times 150$, and the section plots are superimposed with undeformed geometry for better comparison with its original shape. Seven representative cycles (1, 5, 10, 50, 100, 300 and 500) were selected for examining variations of displacement.

In all cases, the peak trabecular bone displacements occurred at the interface in the middle region of the screw hole at the top, and the entrance of screw hole at the bottom for all three stages. The peak displacements of trabecular bone at section A-A at selected cycles for all six models were extracted and are shown in Figure 3.

The maximum and minimum principal strain contours are shown in Figure 4 for VEP models at seven representative cycles.

Peak loading timepoints. At the peak loading timepoints, the difference in displacement between the samples with different BV/TV is apparent. The lower BV/TV samples undergo larger interfacial displacements than higher BV/TV samples, as seen from the displacement contours (Fig. 2a), peak displacements (Fig. 3a) and principal strain contours (Figs 4a and 4b).

At peak loading timepoints, similar displacement contours were observed for models which included VEP and those that were modelled using VE alone. Small differences were, however, observed after the samples had experienced a relatively larger number of cycles and for trabecular bone with low BV/TV. Thus, 15 VEP had slightly higher displacement than the 15 VE cases. The differences between VE and VEP models were negligible at the highest BV/TV considered in the study, as between 35 VE and 35 VEP. As expected, Figure 3a shows that the maximum displacement experienced by trabecular bone increases with the number of cycles. However, this increase was found to be small; the largest increase for the lowest BV/TV sample with a VEP model was 15%. Lower BV/TV in conjunction with viscoplasticity produced larger maximum displacements.

By examining the maximum and minimum principal strain contours (Figs 4a and 4b), we observe that the strain experienced by trabecular bone increases with the number of cycles. It is worth noting that the magnitude of strains in bone during the loading phase were generally below 0.5% and 0.7% for tension and compression, respectively, which are the typically reported yielding strains in the literature.¹⁸⁻²⁰ Another observation is that trabecular bone experiences higher strain in compression than in tension (Figs 4a and 4b). As in the observation about displacements, the magnitude of strain increases with a decrease in the BV/TV of trabecular bone.

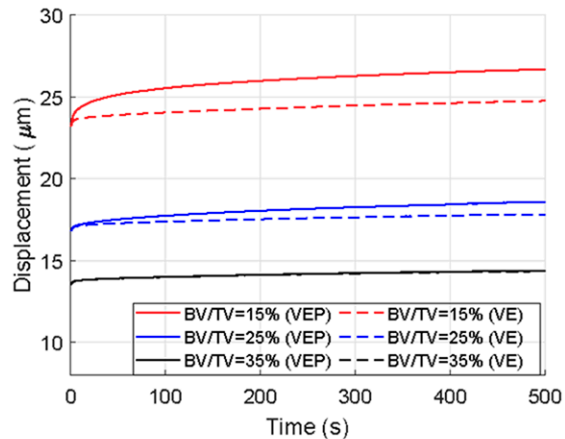


Fig. 3a

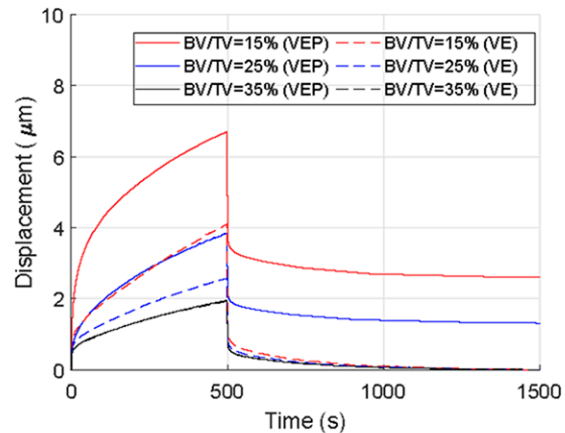


Fig. 3b

Peak displacement of trabecular bone at section A-A for both VE and VEP models when load is at its peak (300 N) (a); when load is zero and after 1000 seconds of recovery (b)

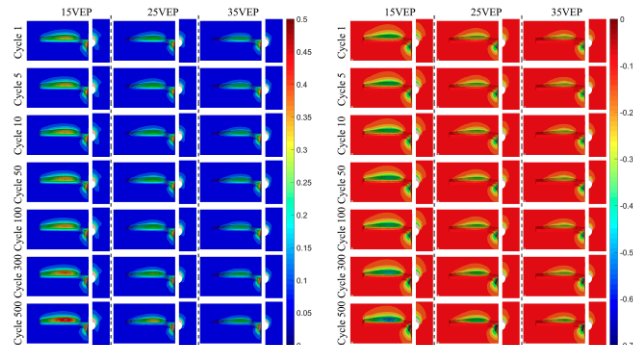


Fig. 4a

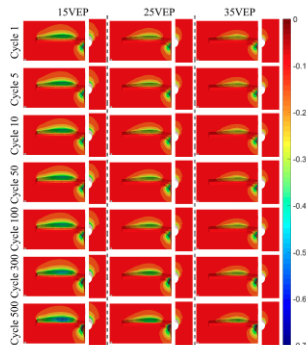


Fig. 4b

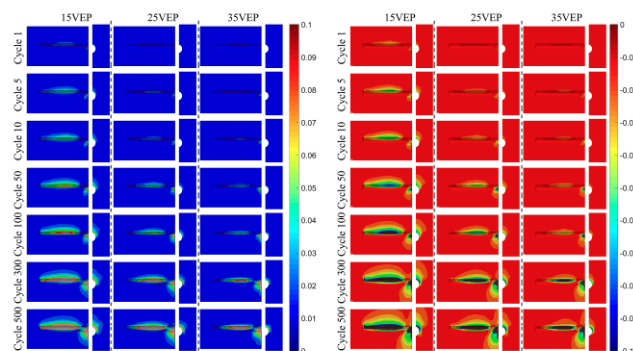


Fig. 4c

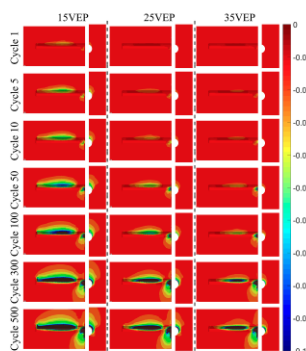


Fig. 4d

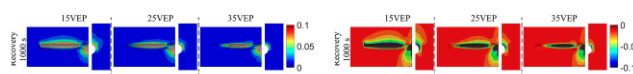


Fig. 4e

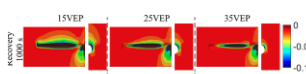


Fig. 4f

Maximum (a, c, e) and minimum (b, d, f) principal strain contours at the symmetry surface and section A-A for seven representative cycles when load at its peak (300 N) (a, b); when load is zero (c, d) and recovery after 1000 seconds (e, f). Strain is expressed as a percentage.

Zero loading timepoints. In the initial cycles, most of the deformation is recovered upon unloading (Fig. 2b). However, as the number of cycles increase, deformations

accumulate with increasing number of cycles at zero load timepoints. This indicates the development of a gap between the screw and the bone. This is also seen when comparing peak displacements, as shown in Figure 3b. As expected, the VEP models have much larger peak deformation upon unloading than VE models, especially for lower BV/TV samples (Fig. 3b). Similar to the loading phase, the displacements of trabecular bone at zero loading timepoints were related to trabecular bone's BV/TV; the deformations were found to increase with a decrease in BV/TV. The largest increase for the lowest BV/TV sample with a VEP model (15 VEP) was > 700% from cycle 1 to 500. It is important to note that at zero load timepoints, there are residual displacements of bone not only when using viscoplastic models but also when using viscoelastic models. These residual displacements cannot be obtained if time-independent elastic properties are used, which require the deformation to recover instantaneously upon unloading.

Figures 4c and 4d show the maximum and minimum principal strain upon unloading with increased number of cycles for VEP models. Most strain is recovered upon unloading (note the difference in scale of the contour plots for peak loading and zero loading timepoints), but residual strains accumulate with the number of cycles and the residual strains are associated with the bone BV/TV. We also found that the accumulation of principal strains, both maximum and minimum, is more rapid for bone with lower BV/TV.

Recovery. All six models were allowed to recover for 1000 seconds under zero force after 500 cycles of loading. As expected, the VE models showed almost complete recovery of displacement, whereas there was residual displacement with VEP models (Fig. 2c). These irrecoverable deformations were found to be related to BV/TV (Fig. 2c); they increased with decreasing BV/TV. The highest irrecoverable deformation was found for bone with

lower BV/TV (Fig. 3b), and irrecoverable deformation was found to be negligible for bone with the highest BV/TV (Fig. 3b). This is also apparent from principal strain contours in Figures 4e and 4f. Bone with lower BV/TV experiences a relatively higher irrecoverable minimum and maximum principal strain, showing that viscoplasticity plays an important role.

Discussion

We found that, in a bone-screw system subjected to cyclical loading, the inclusion of time-dependent properties for trabecular bone predicts separation between the screw and bone, which increases with an increasing number of cycles. Incorporation of viscoplasticity results in larger deformation, some of which is irrecoverable. Interfacial deformation was found to follow a trend based on BV/TV, with porous bone having larger deformations, or larger separation between the screw and the bone.

Numerical simulation of loosening due to mechanical forces in a bone-screw system subjected to cyclical loading has not been possible previously, as a time-dependent material constitutive model of bone has not been included before. A recent multiple-load-creep-unload-recovery experimental study,¹³ followed by the development of time-dependent constitutive models¹⁵ for trabecular bone, has permitted their use in this clinically-relevant study. A number of previous studies, both clinical²¹ and experimental,^{22,23} have reported that the migration of an implant or loosening of a screw is a function of time or the number of cycles. Taylor and Tanner² suggested that the migration of an implant is a mechanical phenomenon, or at least mechanically triggered, rather than a biological process. As demonstrated by previous *in vitro* studies, our simulations show that deformation is a function of the number of cycles for both loading and unloading phases. Inclusion of time-dependent properties implies that deformation accumulates with increasing number of cycles, in contrast to conventional time-independent finite element analyses, in which the deformation or strain remains unchanged with an increasing number of cycles.

The inclusion of time-dependent properties implies that, upon unloading, although a significant proportion of deformation is recovered, residual deformations exist. So, while the screw returns to its undeformed and unstrained configuration, the recovery of the bone deformation lags, and the lag increases with each loading cycle. As would be expected, inclusion of viscoplasticity results in the unloaded deformations being larger due to a proportion being irrecoverable. The latter is apparent when deformations are compared following 1000 seconds of recovery in that the deformations with the non-linear viscoelastic model recover almost entirely.

During the loading phase, the deformations in the bone are forced to follow those of the screw. Consequently,

bone deformations only show a small increase with an increasing number of cycles as the time lag between the bone response and the instantaneous response of the screw increases. At peak loading in the first cycle, there is no difference between deformations from VE and VEP models (Fig. 3). However, with increasing numbers of cycles, differences emerge. Thus, we found that the inclusion of viscoplasticity produces larger deformations not only at zero loading timepoints, but also at peak loading timepoints.

The strong positive relationship between the BV/TV of trabecular bone and its time-independent properties has been previously reported.^{19,24} In general, bone with higher BV/TV has a larger stiffness and yields at larger loads, though it is recognized that the bone's microstructure also has an important role. In other words, denser trabecular bone has a better ability to resist the applied forces and undergoes lower deformations. This trend was consistently observed with the three samples we considered. The deformations at different stages followed a clear trend based on trabecular bone's BV/TV. Porous bone, with lower BV/TV, has higher deformation compared with less porous bone. This is true for loading and unloading timepoints and even for recovery modelled using viscoplasticity. It has also been reported in various studies that implants are more likely to be unstable in bone with low density, such as due to osteoporosis. These studies include *in vitro* experiments,^{22,25,26} finite element simulations^{27,28} and clinical findings.²⁹ Basler et al²² found that displacement was strongly correlated with the initial BV/TV ($r^2 = 0.95$), which implies that it is also related to implant migration. Consistent results are seen in the current study. Screws are more likely to be unstable in bone with a low BV/TV which has higher interfacial deformation, compared with denser bone. In addition, the deformation increases more rapidly with increasing numbers of cycles.

We considered primary stability soon after the operation and before any biologically driven remodelling of bone occurs in a manner similar to several previous computational^{4,7} and *in vitro*^{22,23} studies. Primary stability relies on interlocking and frictional bone-screw contact phenomena. The cycle-dependent deformation results in the screw hole become enlarged. This causes the frictional resistance at the bone-screw interface to reduce with increasing loading cycles. Donaldson et al⁴ reported that, in unilateral external fixators, there exist push-in and pull-out forces that accompany axial loading. These forces, in conjunction with increasing diameter of the screw hole and decreasing frictional resistance, can result in an increased risk of loosening, particularly in low BV/TV bone.

It has been suggested that bone ingrowth and ongrowth occur if the micromovements are $< 40 \mu\text{m}$ to $50 \mu\text{m}$.³⁰ If physiological loads give rise to bone-implant

micromovements of the order of 100 μm to 200 μm , they inhibit the ingrowth of bone, resulting in the formation of fibrous tissue around the prosthesis³¹ and eventual loosening.³² Some previous experiments have shown that the threshold value of micromovement for osseointegration is between 30 μm and 150 μm .³³ Although we considered an idealized system, with a screw inserted in a block of bone, it is tempting to examine quantitative values of the interfacial movements. They are smaller than the threshold value of micromovement required in the formation of a fibrous tissue layer. However, it is important to note that in the idealized system used in this study, the offset at which the load is applied is perhaps similar to that in a locking plate, while devices with a larger offset, such as unilateral fixators, will result in much larger forces at the bone-screw interface. Moreover, it has been shown that deformations increase non-linearly as the external plate or frame bends,⁷ a phenomenon not included in this study. We only applied 500 cycles, as non-linear simulation takes considerable computational resources. Nonetheless, the trends show that the separation continues to increase. While the magnitude of the maximum and minimum principal strains is generally lower than the typically reported values for yield, they are not too far from yield values after 500 cycles of load application, particularly for the lowest BV/TV sample considered. It is also important to note that, while minimum principal strain occurs primarily in a direction radial to the screw, maximum principal strain is in the hoop direction. Steiner et al³⁴ reported that damage to the bone may occur due to the process of inserting the screw itself, with most damage occurring within a 300 μm radial distance of the screw. In this study, we assumed that the screw was inserted into bone without any damage. Consequently, this study is valid with respect to trends rather than actual quantitative values.

This study had limitations. We used single frequency of 1 Hz. It is reasonable to expect that the quantitative results will vary with the choice of frequency.³⁵ However, the trends in the range of frequency that are not too dissimilar to the one selected here, are likely to be maintained. We found a clear trend with variation in BV/TV, but we only considered three samples. A statistical analysis that considers the influence of different BV/TV was not possible. So, while we expect the trend to be generally followed, we deliberately did not develop a relationship with respect to BV/TV. Previous studies on time-independent mechanical properties of bone have shown that, in addition to BV/TV, microstructure plays an important role.³⁶ We expect microstructural anisotropy, in particular, will have a role in time-dependent properties. As the focus of this study was to examine the radial separation at the bone-screw interface, and not slippage due to pull-out forces, the threads of the screws were not included. The threads are likely to reduce loosening due to slippage

when pull-out or push-in forces are applied. However, they generate stress/strain concentrations at the interface which may also accentuate loosening. We only applied 500 cycles; a larger number of cycles would increase the predicted separation. Lastly, time-independent elastic material properties were used for cortical bone and screws. The time-dependent effect on the screw is negligible, but cortical bone will also have time-dependent behaviour. Inclusion of time-dependent behaviour for cortical bone is likely to accentuate screw loosening even further.

The current study is more advanced than the conventional finite element analyses of the mechanics of the bone-screw interface, in which only time-independent material properties that are either elastic,^{16,37} or inelastic,^{4,14} are assigned to bone. However, it does not consider a full bone-fixator construct. The importance of time-dependent effects at the bone-screw interface was discussed at least two decades ago,² but these have not been previously included in models, due to a lack of experimental data and an absence of time-dependent constitutive models for bone. The developed non-linear viscoelastic-viscoplastic constitutive models permit the simulation of time- and cycle-dependent responses to be included in the analysis of bone-screw systems.

We can conclude that the loosening of an implant due to physiological activities can be predicted computationally by employing models that incorporate the time-dependent behaviour of bone. Implants are at a great risk of loosening in osteoporotic patients with a lower BV/TV. We know that secondary healing can be promoted by the application of cyclical loads that cause interfragmentary movement between fractured segments. Clinically, this implies that the need for the application of cyclical loads must be balanced against the risk of loosening before healing occurs.

Supplementary material



Details of the non-linear viscoelastic and non-linear viscoelastic-viscoplastic computational models used, as well as data for each of the three BV/TV values considered.

References

1. MacLeod A, Pankaj P. Computer Simulation of Fracture Fixation Using Extramedullary Devices: An Appraisal. In: Doyle B, Miller K, Wittek A, Nielsen PMF, eds. *Computational Biomechanics for Medicine: Fundamental Science and Patient-specific Applications*. New York: Springer, 2014:87–99.
2. Taylor M, Tanner KE. Fatigue failure of cancellous bone: a possible cause of implant migration and loosening. *J Bone Joint Surg [Br]* 1997;79-B:181–182.
3. Sakaguchi RL, Borgersen SE. Nonlinear finite element contact analysis of dental implant components. *Int J Oral Maxillofac Implants* 1993;8:655–661.
4. Donaldson FE, Pankaj P, Simpson AHRW. Bone properties affect loosening of half-pin external fixators at the pin-bone interface. *Injury* 2012;43:1764–1770.
5. Huiskes R, Chao EYS, Crippen TE. Parametric analyses of pin-bone stresses in external fracture fixation devices. *J Orthop Res* 1985;3:341–349.
6. Clifford RP, Lyons TJ, Webb JK. Complications of external fixation of open fractures of the tibia. *Injury* 1987;18:174–176.

7. MacLeod AR, Simpson AHRW, Pankaj P. Age-related optimization of screw placement for reduced loosening risk in locked plating. *J Orthop Res* 2016;34:1856–1864.
8. Bianco RJ, Arnoux PJ, Wagnac E, Mac-Thiong JM, Aubin CÉ. Minimizing pedicle screw pullout risks: a detailed biomechanical analysis of screw design and placement. *Clin Spine Surg* 2017;30:E226–E232.
9. Bowman SM, Keaveny TM, Gibson LJ, Hayes WC, McMahon TA. Compressive creep behavior of bovine trabecular bone. *J Biomech* 1994;27:301–310.
10. Yamamoto E, Crawford RP, Chan DD, Keaveny TM. Development of residual strains in human vertebral trabecular bone after prolonged static and cyclic loading at low load levels. *J Biomech* 2006;39:1812–1818.
11. Kim D-G, Shertok D, Ching Tee B, Yeni YN. Variability of tissue mineral density can determine physiological creep of human vertebral cancellous bone. *J Biomech* 2011;44:1660–1665.
12. Manda K, Xie S, Wallace RJ, Levrero-Florencio F, Pankaj P. Linear viscoelasticity - bone volume fraction relationships of bovine trabecular bone. *Biomech Model Mechanobiol* 2016;15:1631–1640.
13. Xie S, Manda K, Wallace RJ, et al. Time Dependent Behaviour of Trabecular Bone at Multiple Load Levels. *Ann Biomed Eng* 2017;45:1219–1226.
14. Pankaj P. Patient-specific modelling of bone and bone-implant systems: the challenges. *Int J Numer Method Biomed Eng* 2013;29:233–249.
15. Manda K, Wallace RJ, Xie S, Levrero-Florencio F, Pankaj P. Nonlinear viscoelastic characterization of bovine trabecular bone. *Biomech Model Mechanobiol* 2017;16:173–189.
16. MacLeod AR, Pankaj P, Simpson AHRW. Does screw-bone interface modelling matter in finite element analyses? *J Biomech* 2012;45:1712–1716.
17. MacLeod AR, Simpson AHRW, Pankaj P. Reasons why dynamic compression plates are inferior to locking plates in osteoporotic bone: a finite element explanation. *Comput Methods Biomech Biomed Engin* 2015;18:1818–1825.
18. Morgan EF, Keaveny TM. Dependence of yield strain of human trabecular bone on anatomic site. *J Biomech* 2001;34:569–577.
19. Levrero-Florencio F, Margetts L, Sales E, et al. Evaluating the macroscopic yield behaviour of trabecular bone using a nonlinear homogenisation approach. *J Mech Behav Biomed Mater* 2016;61:384–396.
20. Bayraktar HH, Keaveny TM. Mechanisms of uniformity of yield strains for trabecular bone. *J Biomech* 2004;37:1671–1678.
21. Born CT, Karich B, Bauer C, von Oldenburg G, Augat P. Hip screw migration testing: first results for hip screws and helical blades utilizing a new oscillating test method. *J Orthop Res* 2011;29:760–766.
22. Basler SE, Traxler J, Müller R, van Lenthe GH. Peri-implant bone microstructure determines dynamic implant cut-out. *Med Eng Phys* 2013;35:1442–1449.
23. Bianco RJ, Aubin CE, Mac-Thiong JM, Wagnac E, Arnoux PJ. Pedicle screw fixation under nonaxial loads: a cadaveric study. *Spine (Phila Pa 1976)* 2016;41:E124–E130.
24. Zysset PK. A review of morphology-elasticity relationships in human trabecular bone: theories and experiments. *J Biomech* 2003;36:1469–1485.
25. Johnston TL, Karaikovic EE, Lautenschlager EP, Marcu D. Cervical pedicle screws vs. lateral mass screws: uniplanar fatigue analysis and residual pullout strengths. *Spine J* 2006;6:667–672.
26. Zhu Q, Lu WW, Holmes AD, et al. The effects of cyclic loading on pull-out strength of sacral screw fixation: an in vitro biomechanical study. *Spine (Phila Pa 1976)* 2000;25:1065–1069.
27. Wirth AJ, Müller R, Harry van Lenthe G. The discrete nature of trabecular bone microarchitecture affects implant stability. *J Biomech* 2012;45:1060–1067.
28. Donaldson FE, Pankaj P, Cooper DML, et al. Relating age and micro-architecture with apparent-level elastic constants: a micro-finite element study of female cortical bone from the anterior femoral midshaft. *Proc Inst Mech Eng Part H* 2011;225:585–596.
29. Galbusera F, Volkheimer D, Reitmaier S, et al. Pedicle screw loosening: a clinically relevant complication? *Eur Spine J* 2015;24:1005–1016.
30. Taylor M, Prendergast PJ. Four decades of finite element analysis of orthopaedic devices: where are we now and what are the opportunities? *J Biomech* 2015;48:767–778.
31. Pilliar RM, Lee JM, Maniopoulos C. Observations on the effect of movement on bone ingrowth into porous-surfaced implants. *Clin Orthop Relat Res* 1986;208:108–113.
32. Viceconti M, Muccini R, Bernakiewicz M, Baleani M, Cristofolini L. Large-sliding contact elements accurately predict levels of bone-implant micromotion relevant to osseointegration. *J Biomech* 2000;33:1611–1618.
33. Kadir A, Rafiq M. *Computational Biomechanics of the Hip Joint*. Springer Science & Business Media, 2014.
34. Steiner JA, Ferguson SJ, van Lenthe GH. Screw insertion in trabecular bone causes peri-implant bone damage. *Med Eng Phys* 2016;38:417–422.
35. Xie S. Characterisation of time-dependent mechanical behaviour of trabecular bone and its constituents (PhD Thesis). The University of Edinburgh Research Archive, 2018.
36. Steiner JA, Ferguson SJ, van Lenthe GH. Computational analysis of primary implant stability in trabecular bone. *J Biomech* 2015;48:807–815.
37. Goffin JM, Pankaj P, Simpson AH. The importance of lag screw position for the stabilization of trochanteric fractures with a sliding hip screw: a subject-specific finite element study. *J Orthop Res* 2013;31:596–600.

Funding Statement

- We gratefully acknowledge the financial support of the EPSRC [Grant EP/K036939/1].

Author Contributions

- S. Xie: Designing and conducting the study, Analysing the data, Drafting the manuscript.
- K. Manda: Developing the algorithm used in the study.
- P. Pankaj: Designing the study, Analysing the data, Critically revising the manuscript.

Conflict of Interest Statement

- None declared

© 2018 Author(s) et al. This is an open-access article distributed under the terms of the Creative Commons Attribution licence (CC-BY-NC), which permits unrestricted use, distribution, and reproduction in any medium, but not for commercial gain, provided the original author and source are credited.